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Review

Climate change and dengue fever transmission in China: Evidences and challenges

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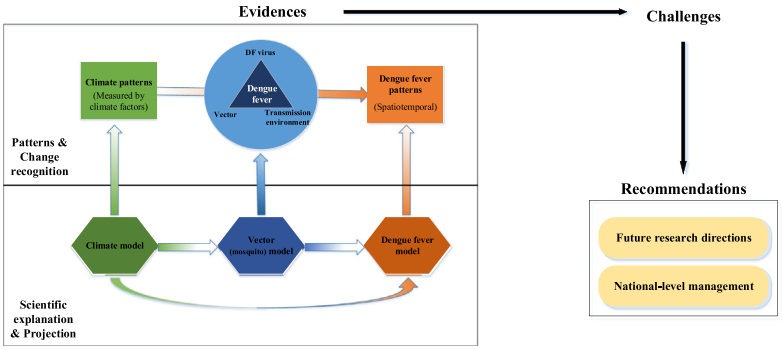
HIGHLIGHTS

- Climate change may bring increased risk of DF to China, especially to its south and southeast coast regions.
- Projection of DF under climate change is related to the development of weather-based DF model, vector and climate models.
- Lack of national-level DF model in China and uncertainties in vector model and climate model are challenges.
- Promoting interdisciplinary collaboration and further developing public health education are recommended for China.

GRAPHICAL ABSTRACT



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ABSTRACT

Dengue Fever (DF) has become one of the most serious infectious diseases in China. Dengue virus and its vector (*Aedes* mosquito) are known to be sensitive to climate condition. Climate impacts DF through affecting three essential bioecological aspects: DF virus, vector (mosquito) and DF transmission environment. Weather-based DF model, mosquito model and climate model are the three pillars to help the prediction of DF distribution. Through a systematic review of literature between 1980 and 2017, this paper summarizes empirical evidences in China on the impact of climate change on DF; it further reviews the related DF incidence models and their findings on how changes in weather factors may impact DF occurrences in China. Compared with some well-known research projects in the western countries, there is a lack of knowledge in China regarding how the spatiotemporal distribution of DF will respond to climate change. However, being able to predict DF distribution is key to China's efforts to prevent and control DF transmission. We conclude this paper by recommending four focused areas for China: promoting more advanced research on the relationship between extreme weather events and DF, developing regional-specific models for the high risk regions of DF in south China, encouraging interdisciplinary collaboration between climate studies and health services, and enhancing public health education and management at national, regional and local levels.

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1. Introduction

After malaria, Dengue Fever (DF) is the second-most serious infectious disease worldwide in terms of mortality and morbidity (Wu et al., 2010). DF is an acute infectious disease caused by four serotypes of dengue virus (DENV-1 to DENV-4), mainly transmitted to humans by *Aedes aegypti* and *Aedes albopictus*. DF is prevalent in tropical and subtropical regions, infecting about 390 million people annually. It is considered as an endemic or epidemic disease in nearly 119 countries, many of which are in Asia (Bhatt et al., 2013; Guzman et al., 2010).

The earliest recorded DF case in China was in the Yangze River Basin in the late 19th century (Luo, 2003). In the early 1940s, sporadic cases of DF were reported in China's southeast coastal regions (Mao and Zhang, 2007). The first outbreak of DF occurred in Foshan City, Guangdong Province in 1978. From 1978 to 1991, DF cases were mainly concentrated in Guangdong Province and Hainan Province. After 1990, DF spread gradually from the southeast coastal regions (e.g. Guangdong Province) northwards, reaching provinces such as Yunnan, Zhejiang, and Fujian (Xiong and Chen, 2014). Until 2008, a total of 677,446 DF cases with 626 deaths have been reported (Qin and Shi, 2014). In 2014, the unprecedented outbreak of DF in Guangzhou City accounted for more than 30,000 cases (Sang et al., 2015). DF is currently included on the list of serious infectious diseases in China (Wu et al., 2010). With rapid urbanization and continuous growth of international tourism in China, the transmissions of infectious disease are faster than ever. Without effective measures, DF may turn into an endemic disease in China's south and southeast coastal regions where the climate is suitable for virus survival and transmission.

The outbreak and transmission of DF are related to a number of risk factors, including dengue virus' presence and vitality (Zhang et al., 2005), mosquitoes' vectorial behavior and capacity (Helmersson et al., 2016), climate or weather conditions (Lu et al., 2009; Wang et al., 2014), human immunity (Endy et al., 2011), and human activity (Tian et al., 2016). However, studies found that the impacts of climate factors on DF are more significant than other factor (Earnest et al., 2012; Hales, 2012; Hales et al., 1996).

With global warming, DF occurrence seasons in China may become longer and climatic conditions are likely to become suitable for DF virus in more regions. DF has been prevalent in China mostly during June to October, with spring and winter as seasons of sporadic occurrence (Wu et al., 2010). Ample sunshine and precipitation in summer provide abundant breeding places for mosquitoes and therefore creating favorable conditions for DF occurrence. A recent research suggested that global warming aggravate the prevalence of DF, as it brings warmer and wetter spring and winter seasons favorable for dengue virus and mosquitoes (Yi et al., 2014). Between 2005 and 2013, DF occurs in most provinces in China (Yue et al., 2015) (Fig. 1). In 2014, a total of 23 out of 34 provinces have reported DF cases (Beijing Youth Daily, 2014). Moreover, the time interval between DF outbreaks has shortened gradually since 2005. All these may suggest that DF is developing from an imported epidemic disease into an endemic disease, especially in the tropical and subtropical regions of China.

Literature reported researches conducted in different countries (e.g. Malaysia and Brazil) that examined the relationship between DF and climate factors (Hii et al., 2016; Limkittikul et al., 2014; Morin et al., 2013; Pang and Leo, 2015; Viana and Ignotti, 2013). As for the studies of China, the magnitude of the relationship has not been adequately addressed. Furthermore, the overall impact of climate change on DF transmission and distribution that involves simultaneous changes in multiple weather factors is less known or investigated. There is a need for national level modeling and prediction of DF distribution in China across space and through time. Through a survey of scientific studies published since 1980 that examined the relationship between climate change and DF in China, this paper addresses the potential impacts of climate change on DF in China, reviews the related modeling and projection of DF based on climate change, and discusses how China can achieve better DF disease control and management under climate change.

2. Research design

The focus of this research is to survey literature for scientific evidences on the impact of climate change on DF distribution in China, and to examine the status of and needs for modeling and prediction of DF in China considering climate change. Climate change includes changes in climate factors and extreme weather events, both of which can affect the distribution of DF. Climate change affects DF transmission through impacting its three essential bioecological aspects: the virus, the vector, and transmission environment (Wu et al., 2016). Therefore, understanding the dynamics of DF under climate change calls for proper modeling and prediction of climate change, that of vectorial (mosquito) abundance and capacity, and that of DF occurrence under certain weather conditions, namely climate model, vector (mosquito) model, and weather-based DF model. We constructed a framework (Fig. 2) named “Tri-model Supported Prediction of Dengue Fever Distribution and Patterns” in order to illustrate the connections between the various elements. Prediction of dengue virus (DENV) transmission and its spatiotemporal patterns must be based on appropriate weather-based DF model, mosquito model and climate model. Weather-based DF model describes the relationship between DF incidence and climate factors. Weather-based DF model serves as the foundation for predicting the spatiotemporal patterns of DF distribution. Mosquito model quantifies the dynamics of mosquito distribution and population, which is closely related to weather conditions. Climate model uses quantitative methods to simulate the interactions of the important drivers of climate (GOESSP, 2011). Climate model not only generates predictions of climate patterns and dynamics of weather conditions but also provides inputs for mosquito model, which will produce outlooks of mosquito abundance and vectorial capacity across space and through time. Projection of DF refers to predicting DF distribution or spatiotemporal patterns based on weather-based DF model when climate factors and their magnitude as well as the related change in mosquito activity are considered. Hence,

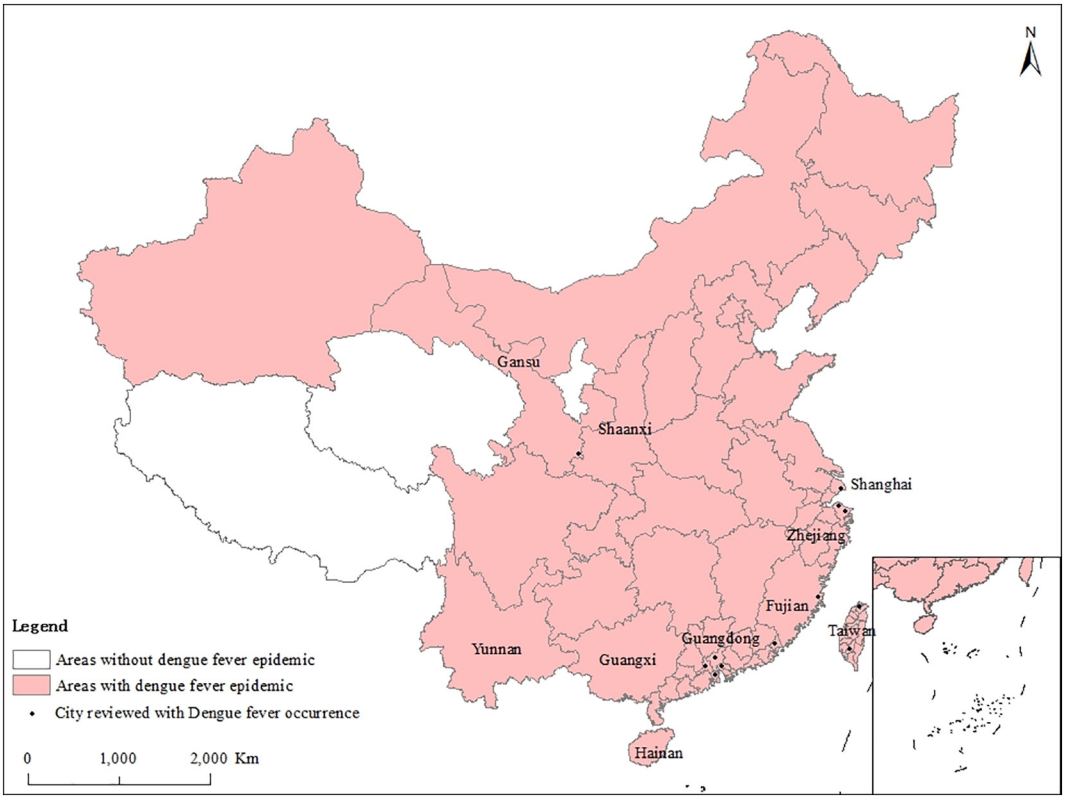

Fig. 1. Province-level Dengue Fever distribution in China (Note: Map was created using the DF data reported in Yue et al., 2015).

the overall prediction of DF distribution patterns, despite of its emphasis on patterns and change prediction, is built upon scientific knowledge of the mechanisms that can explain and predict climate change, mosquitos' vectorial capacity, and DF occurrence. Our selection of literature and design of this review research are guided by this framework as illustrated in Fig. 2.

Considering the first recorded outbreak of DF case in China was reported in 1980 (Guan and Huang, 2000), our literature survey covers papers and reports related to DF in China that were published from 1980 to 2017. Following the framework above (Fig. 2), the keywords defined by three sets of terms were used to screen the literature; the returned results must contain keywords from at least one of three sets (Table 1). The first set describes patterns and change recognition of DF transmission driven by climate change in China. The terms are related to climate change and the three aspects of DF in China. Keywords included climate factors such as temperature, humidity and precipitation, extreme weather events such as EI Nino, typhoon, flood and drought, and dengue fever, dengue virus, mosquitoes, transmission, outbreak/occurrence, China, as well as Chinese provinces (e.g. Guangdong). The second set of terms describes models of DF transmission in China, which

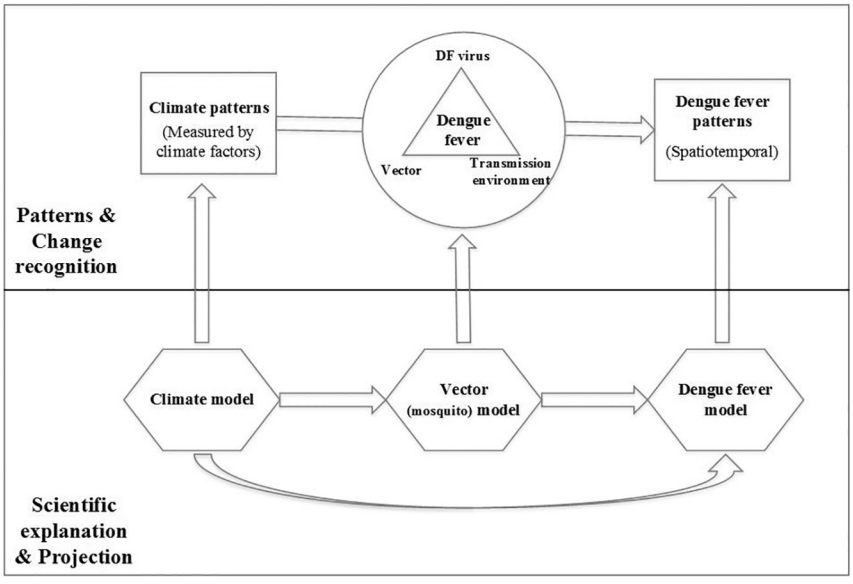

Fig. 2. Tri-model supported prediction of Dengue Fever distribution and patterns.

Table 1
The list of keywords used to screen the literature.

Sets	Categories	Keywords
Set 1: Impact of climate change on dengue fever	Three aspects of dengue fever transmission	dengue virus, DENV, vectors, mosquito, *Aedes aegypti*, *Aedes albopictus*, transmission, environment, outbreak, occurrence
	Weather factors	climate factor, weather factor(e.g. temperature, humidity, precipitation, wind, air pressure), extreme weather events(e.g. EI Nino, typhoon, flood and drought)
	Geographical location	China, provinces of China (e.g. Guangdong, Fujian, Zhejiang), Taiwan, cities of China (e.g. Guangzhou, Zhongshan, Cixi)
Set 2: Model of climate change on dengue fever	Weather-based dengue fever model	dengue fever, model, transmission, climate, weather, Poisson, regression
	Mosquito model	mosquito, model, climate, weather, population, quantitative/qualitative model
	Climate model	Climate model (e.g. BNU_ESM), scenario, RCP2.6, RCP4.5, RCP6.0, RCP8.5
Set 3: Projection of dengue fever		Projection, prediction, dengue fever incidence, future climate condition

involved models of DF incidence and climate factors, mosquito models and climate models. Keywords included DF model, mosquito population model, climate model (e.g. BNU_ESM), and China. The third set of terms describes projections of DF transmission and distribution patterns in China. Keywords included projection of mosquito population, prediction of DF incidence, and China. A comprehensive literature search was conducted using Google Scholar (http://scholar.google.com), Web of Science/Knowledge, PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Baidu Scholar (http://xueshu.baidu.com), and CNKI (http://www.cnki.net/).

Fig. 3 showed the process of literature screening. Using the search keywords, we initially identified a total of 874 publications. Based on the inclusion criteria that a study must be in China (including Chinese Autonomous Regions, Hong Kong, Macau and Taiwan), 697 studies were kept for further review. In the second round of screening, 435 additional articles were excluded after further examination of title and abstract. The focus of these excluded articles was on virological, genetic or serological aspects of DF and treatment. Finally, through reading full text of the remaining papers, a total of 81 publications were selected for this literature research. The majority of these articles examined the relationship between climate change and DF transmission in China. Supplementary Table 2 lists 49 articles selected for evidences, which are grouped based on three perspectives including impact, model and projection of climate change and DF exclusively in China. In addition, a small number of selected articles with an area focus other than China were included in the literature study due to their close relevance to the topics covered by this review research – the challenges for China in order to better understand and predict the impact of climate change on DF and our recommendations.

3. Impact of climate change on DF in China

3.1. Impact of weather factors on DF

Climate change refers to statistical shifts of climate conditions over a long period of time, including alternations of one or more weather factors such as temperature, precipitation, humidity, wind velocity, and air pressure (Wu et al., 2016). These changes impact incidence of DF through affecting the survival, replication, development or distribution of dengue virus and mosquitoes, as well as the means and process of dengue transmission. In this section, we provide a systematic literature summary of the impacts of weather factors on DF from three bioecological aspects – impact on dengue virus, impact on dengue vector (mosquito), and impact on dengue transmission environment (Supplementary Table 1).

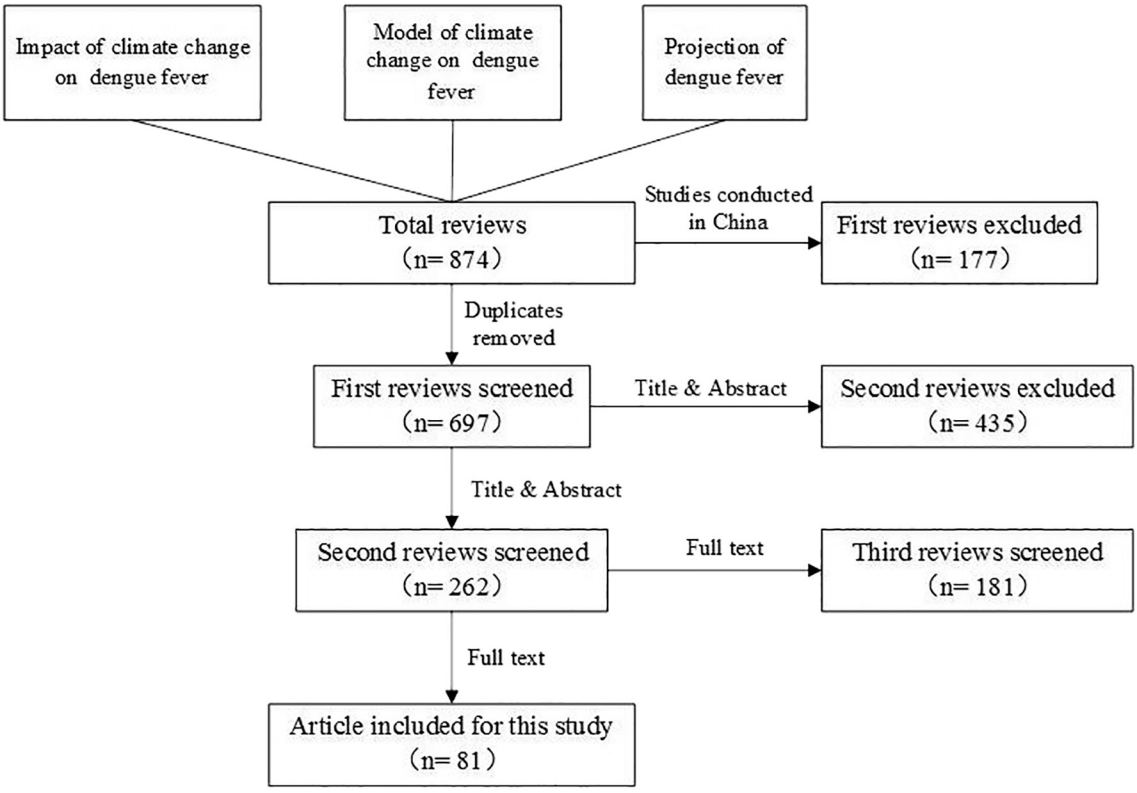
Impact of climate change on dengue fever
Model of climate change on dengue fever
Projection of dengue fever
Total reviews (n= 874)
Studies conducted in China
First reviews excluded (n= 177)
Duplicates removed
First reviews screened (n= 697)
Title & Abstract
Second reviews excluded (n= 435)
Title & Abstract
Second reviews screened (n= 262)
Full text
Third reviews screened (n= 181)
Full text
Article included for this study (n= 81)

Fig. 3. Flowchart of the literature search.

Dengue virus (DENV) is sensitive to change of weather factors, especially temperature. The appropriate temperature for dengue virus to replicate in *Aedes* species is a certain range (Fan and Liu, 2013). Previous studies suggested that higher temperature helps dengue virus survive and increases their replication (Lu et al., 2009; Tseng et al., 2009). Rising temperature can accelerate the reproduction and shorten extrinsic incubation period (EIP) of dengue virus, which is beneficial to DF transmission. Zeng (2002) found that the EIP of DENV-1 reduces from 12 days at 30 °C to 7 days at 34 °C.

Aedes aegypti, the vector of DENV, does not regulate its body temperature, which is directly dependent on ambient temperature. So it is sensitive to a certain climate condition (Elbers et al., 2015). Studies have shown that weather factors including temperature, precipitation, humidity and wind velocity can affect the survival, development and reproduction of mosquitoes (Almeida et al., 2005; Chen et al., 2002; Wu et al., 2011; Yi et al., 2003b). Temperature may affect mosquitoes from multiple aspects. First, temperature can affect different stages of mosquito's life cycle. A study showed that during mosquito development period, the duration and survival rate are different under different temperatures; in cold environment, incubation period is longer (Zhong and He, 1988). Second, mosquito density is related to temperature. According to a study in Fuzhou city, mosquito density increases as temperature becomes high; but when temperature is above 32 °C, mosquito density decreases significantly (Zheng et al., 2001). Third, female mosquitoes require a blood meal for ovarian development, and their biting behavior is influenced by temperature. A study in Yunnan Province found that biting activities of mosquitoes are limited to temperature between 15 °C and 35 °C, and the optimal temperature range is 25 °C~30 °C (Zhang and Zhang, 1994). Fourth, temperature change may bring changes in the spatiotemporal range of mosquito distribution. As winter temperature in Hainan Province continues to increase, mosquitoes may be active year around (Chen et al., 2002). A study on the distribution of *Aedes albopictus* found that mosquitoes had extended their habitats to new areas in northwest China such as the western area of Shaanxi Province and Liangdang County of Gansu Province (Shi and Zhang, 2012). Fifth, changes in temperature can impact mosquitoes' flying distance. Under the suitable temperature range from 20 °C to 27 °C, a mosquito can fly more than 400 m. When temperature is below 18 °C, the flying distance is generally within 50 m (Jing et al., 1998). Precipitation is necessary to provide essential breeding sites for mosquitoes. Yi et al. (2003b) developed a DF model and proved that the mosquito density in Chaozhou City of Guangdong Province is positively associated with precipitation. Humidity, related to both temperature and precipitation, also affects DF incidence through altering mosquito behaviors. A study found that from dry to wet season, mosquito bites on human can increase from 19 to 60 bites/(person· hour) (Almeida et al., 2005). Wind velocity may be inversely associated with mosquito density. A study conducted in Guangzhou City demonstrated that wind velocity can suppress a mosquito's fly and thus can impact its oviposition (Wang et al., 2014).

DF transmission environment in this paper refers to the spreading of DF rather than DF transmission mechanism. Temperature, precipitation, humidity and air pressure were considered as major weather factors for DF transmission by many studies (Liu et al., 2017; Lu et al., 2009; Sang et al., 2014). Some studies have identified an obvious correlation between temperature and DF incidence in China. For example, using the classification and regression tree (CART) model, Liu et al. (2017) found that temperature and diurnal temperature range play critical roles in DF transmission in Zhongshan City, Guangdong Province. Temperature at a lag of 2 months was positively associated with DF incidence, whereas diurnal temperature range had an inverse association with DF transmission at a lag of 1 month. In addition, a study suggested that precipitation plays a key part in explaining the dynamics of DF incidence in Guangzhou City. More precipitation was a strong predictor for increased DF cases (Xu et al., 2017). Furthermore, a previous study showed that in Guangzhou City, temperature, humidity and precipitation were positively associated with DF incidence, while air pressure had a negative effect on DF at a lag of 3 months (Sang et al., 2014).

The studies on the relationship between weather factors and DF are abundant; but the findings on the effects are not always consistent. Studies in different areas produced outcomes different from each other with regard to the effects of the same weather factors. For example, a study in Taiwan found that mean, maximum and minimum temperatures were positively associated with DF incidence in Taibei City. In contrast, a negative effect of mean, maximum and minimum temperature on DF was identified in Kaohsiung City, Taiwan (Chen et al., 2010). Yet, one study in Cixi City, Zhejiang Province reported no correlation between DF and temperature (Yang et al., 2009). Similarly, no correlation was found between precipitation and DF incidence in Zhongshan City (Liu et al., 2017), but there was a highly positive relationship between precipitation and DF in Guangzhou City (Sang et al., 2015). These studies collectively may suggest that the climate-DF association depend largely on local climate condition unique to a particular study area. Moreover, research findings were different in the same study area but at different study periods. For example, a study in Guangzhou City from 2001 to 2006 showed that humidity is positively related to DF incidence (Lu et al., 2009), while another study in Guangzhou City during 2011–2014 found humidity has a negative effect on DF (Chen et al., 2016).

A limited change of certain weather factor may lead to epidemics of DF. For example, a small change in temperature, as a trend of global change, can extend the suitable habitat regions for DF vectors and alter DF distribution drastically. Using GIS, Yu et al. modeled a DF epidemic and found that as winter temperature increases, over half of the areas in Hainan Province would allow year-round DF transmission by 2050 (Yu et al., 2005). A study in Taiwan showed that with every 1 °C increase of monthly average temperature, the population at risk for DF would increase from 3,966,173 to 7,748,267 (Wu et al., 2009). However, rising temperature does not always increase DF incidence, because there is a temperature threshold range for DF incidence (Fan and Liu, 2013). Increased temperature in already warm regions may have negative impacts on DF transmission through decreasing virus vitality and limiting mosquito reproduction and development.

3.2. Impact of extreme weather events on DF

Extreme weather events include regional or local scale meteorological hazards and global scale extreme events (Wu et al., 2016). With global warming, the frequency and intensity of extreme weather events have changed significantly in China. Extreme weather events can change DF incidence through impacts on dengue virus, mosquitoes or transmission environment. El Niño is one of the most well-known global-scale extreme weather events. A study conducted in Guangdong Province from 2005 to 2011 found that El Niño/Southern Oscillation (ENSO) was associated with DF transmission. They found that higher temperature that is associated with El Niño/ENSO in Guangdong Province was positively correlated with DF incidence (Fan et al., 2014). Another study found that the increased humidity in Kaohsiung city, Taiwan in 2005 that was caused by El Niño/ENSO was more conducive to mosquitoes growth and breeding (Lai, 2011).

Extreme weather events at the regional or local scale in China can also impact DF incidence. These events include drought, flood, typhoon and heat wave. A study suggested that drought help reduce DF incidences by limiting the number of mosquito breeding sites and the growth environment of mosquitoes (Huang et al., 2000). However, Lee and Yu suggested possible connection between drought and high DF occurrence; Kaohsiung City underwent two DF occurrences in 2002 and 2014, and these two years saw severe droughts. Especially in 2014, Kaohsiung suffered from the highest number of DF cases in history (Lee and Yu, 2015). In addition, heat waves were found to be associated with increased DF incidences and associated deaths, particularly

in the metropolitan regions of the Pearl River Delta in China (Du et al., 2013).

Similar extreme weather events may cause different health impacts, related to the magnitude of change in climate factors. For example, typhoon in south and southeast Asia brings massive precipitation and high humidity, often leading to increase in mosquitoes breeding environment (Lai, 2011). Conversely, excessive precipitation and sharp drop of temperature caused by typhoon were found to reduce DF infections (Hsieh and Chen, 2009). Similarly, a study showed that flood tends to lead to an increase in DF incidences due to increased mosquito habitats and thus high mosquito density (Fan and Liu, 2013). However, flood can also damage mosquito habitats and flush away their eggs and larvaes, which could result in a decrease in DF incidences (Gao et al., 2016).

In summary, empirical studies on the relationship between climate change and the three aspects of DF transmission are abundant, especially concerning DF vector. However, there is a lack of investigations on the correlation between DF incidence and extreme weather events, especially in the mainland. Moreover, there is a clear need for a systematic prediction on how changes in extreme weather events may lead to spatiotemporal changes in the distribution of DF in China.

4. Modeling and projection of DF in China

With global climate change, modeling of DF under the impact of changing weather factors has become more challenging. In addition to understanding and modeling climate change, we must predict how DENV vector responds to changes in climate and how these changes will impact *Aedes* mosquitoes' vectorial capacity. Therefore, DF model, mosquito model and climate model are essential for modeling and projecting the spatial and temporal patterns of DF transmission (Fig. 2).

In China, there are a number of DF models on the relationship between DF and weather variables. It is important to notice the variations across these models. These variations are mostly due to a lack of scientific agreement regarding the nature of the relationship between climate factors and DF. Furthermore, the different models are based on different distributional assumptions regarding if distribution of DF cases follows normal or Poisson rule and they consider different spatial or temporal characteristics of both DF cases and climate factors. For example, Sang et al. (Sang et al., 2015) used Poisson regression model for time series analysis to determine the association between weather variables (minimum temperature, precipitation) and DF in Guangzhou City during 2006–2014. Xu et al. (2017) employed structural equation model to explore the direct and indirect effects of temperature and precipitation on DF occurrences; they further used generalized additive model (GAM) and zero-inflated GAM for an ecological model of DF. Another study developed a DF model using GAM with Poisson link function by considering key weather factors in Guangzhou City during January 1998 to December 2012 (Li et al., 2017). A study in Zhongshan City of Guangdong Province used negative binomial regression model with a log link function to analyze the relationship between weekly DF cases and climate factors (Zhang et al., 2016).

Understanding the mechanism for mosquito population change is key to the management and control of DF Transmission. Chinese researchers have adopted both qualitative and quantitative approaches to develop mosquito models. Spatial analysis and data fusion technologies such as geographical information systems (GIS) and remote sensing (RS) have been used to produce qualitative projection of the presence and distribution of mosquitoes (Yi et al., 2003a). Quantitative mosquito modeling considering climate conditions can be grouped into two categories: statistical population model and mechanistic population model (Kendall et al., 2008). The former aims to establish a mathematical relationship between the population size of mosquito and the measurements of certain climatic factors, a relatively often-seen approach in China (Yu, 2013; Zhou et al., 2014c). For example, a study in Shanghai City used multiple stepwise regression method to examine the relationship between *Ae. Albopitus* density and climate factors (Zhou et al., 2014c). The latter type of mosquito model described the intrinsic biological mechanism of how mosquito's lifecycle is impacted by climate factors; there are not many such models in China. Jia et al. used data of monthly Container Index (CI) of *Ae. albopitus* in Shanghai City and Guangzhou City and developed a generic climate-driven mechanistic population model with diapauses (Jia et al., 2016).

Recent years have seen some important development of climate models in China. Five Chinese Climate/Earth System Models (BNU-ESM, BCC-CSM1–1, FGOALS-s2, FGOALS-g2 and FIO-ESM) were incorporated into the Coupled Model Intercomparison Project Phase 5 (CMIP5) (Zhou et al., 2014b). The projection of future climate change was performed under four scenarios of greenhouse gas emission. These four Representative Concentration Pathway (RCP) scenarios describe the possible range of radiative forcing of greenhouse gases in 2100, including a rigorous mitigation scenario (*RCP2.6*), two intermediate scenarios (*RCP4.5* & *RCP6.0*) and one scenario with very high emission (*RCP8.5*) (IPCC, 2014a). Projections of climate (e.g. temperature & precipitation) under the four RCP scenarios for different time spans (e.g. 2020s, 2050s, and 2080s) are different (Xu and Xu, 2012), which will affect the incidence of DF to different extent, including its occurrence and distribution.

Built upon the different weather-based DF models, mosquito models and climate models, projections of DF distribution and its spatiotemporal patterns in China were made by a number of studies (Chen et al., 2002; Du et al., 2015; Fan, 2013; Yu et al., 2005). Incorporating climate model and DF model to predict DF distribution, Du et al. (2015) conducted a study in South China including Guangxi, Guangdong and Hainan provinces and predicted that under RCP4.5 greenhouse gas emission scenario, compared with the average situation during 1997–2012, the number of days per year that are suitable for DF transmission will increase by 10, 15 and 20 days in 2020s, 2050s and 2080s respectively and the areal size of regions prone to DF epidemic all year round will increase by 3962 km^2, 5436 km^2 and 8260 km^2 respectively. Under RCP8.5 scenario, the same study suggests that the average number of days per year that are amicable for DF transmission will increase by 15, 25 and 40 days in 2020s, 2050s, and 2080s and the DF all-year-round epidemic region will increase by 4536 km^2, 8780 km^2 and 20,680 km^2 respectively (Du et al., 2015). Another approach to predict DF distribution relies heavily on projection of mosquito population and distribution based on mosquito model and climate model. For example, a study showed that under RCP6.0 scenario, there would be an additional 1382.5 km^2 highly suitable habitats for *Aedes albopictus* in China in 2030 and 2516.6 km^2 in 2050; under RCP8.5, the increase would be 2029.0 km^2 and 2791.1 km^2 respectively. Moreover, an additional 691.2 km^2 would become DF risk areas by the year 2030 under RCP6.0 and 1602.9 km^2 under RCP8.5; 1136.7 km^2 and 1394.4 km^2 would be added to DF risk areas under RCP6.0 and RCP8.5 by 2050 (Fan, 2013).

China is a developing country with a vast territory, population, and economy as well as complex topography and diverse climates. There exist some unique challenges for studying climate change and its impact on DF transmission in China. First, climate and ecological characteristics vary across different regions, and therefore a DF model established in a study area tends to be regionally specific (Xu et al., 2017; Zhang et al., 2016). Second, the widespread and indiscriminate abuses of pesticides have led to mosquito resistance throughout the country (Wu et al., 2010), which increases the uncertainty in modeling population and distribution of mosquitoes. Third, there are some uncertainties for climate models. The uncertainty regarding emission magnitude impacts the accuracy of climate models. For China particularly, the implementation of two-child policy since 2016 is likely to bring complex effects on population and economic growth (Gong et al., 2016), which may increase uncertainty in emission prediction (Naish et al., 2014). Uncertainties in the prediction of a climate model also stem from the uncertainties in model inputs, which may include various aspects, such as volcanoes, aerosols, and land use/cover.

5. Discussion

Climate factors impact DF incidence and distribution in a complex way. But the impact can be more complicated when anthropogenic factors enter the picture. First, imported DF caused by human activity (e.g. travel) can pose a more severe threat for DF outbreak in regions with favorable weather conditions. For example, an epidemiological study found evidence that when climate condition is suitable, imported cases from Southeast Asia can initiate DF outbreaks in Dongguan City, Guangdong Province (Peng et al., 2012). People in non-endemic regions where mosquito vector is established may be at risk of DF outbreak due to the introduction of virus as a result of globalization, especially through international travel. A DF outbreak in 2004 in Cixi City and Ningbo City, Zhejiang Province, was believed to be associated with a traveler who returned from Thailand, a country under the attack of a DF epidemic at that time (Wiwanitkit, 2005; Xu et al., 2007). Second, cities, being the spatial focal for most people's daily activities nowadays, may serve as the best places for DF transmission and outbreak. In subtropical Taiwan, the level of urbanization was found to be significantly associated with DF risk; urbanization was included in models to predict DF infections from 2003 to 2006 (Wu et al., 2009). Last, as the scale of human-initiated projects continues to grow, the potential of such anthropic programs to create significant impact on DF incidences cannot be overlooked. A previous study showed that urban environmental changes, especially changes in surface area of man-made lakes, could substantially alter DF transmission (Tian et al., 2016). The impact of mega projects such as the Three Gorges Dam on DF when climate change is considered has yet to be studied.

Nevertheless, human beings can play an active role in DF control and prevention. For example, pesticide application is a usual means to control vectors through eliminating mosquitoes from the breeding sites. Some cost-effective bio-control pesticides such as *Bacillus thuringiensis* are believed to be promising in some regions without environment impact (Wang and Wang, 2000). A mosquito monitoring system incorporating Breteau index, house index, and container index to examine mosquito larvae has been used in some high-risk regions for DF in China (such as Hainan Province and Guangxi Province) and has produced encouraging results (Tan et al., 2004; Xie and Fu, 2007).

DF is a weather-sensitive infectious disease. Selecting appropriate DF models, mosquito models and climate models are not trivial tasks in order to accurately project the occurrence and distribution of DF in China. For DF models, studies considering long time period (such as 14 years as in (Li et al., 2017)) may help reveal a more complete pictures of DF transmission across space and through time. Additionally, it is important to understand the potential impact from simultaneous changes of multiple climate factors. For the study of mosquito models, Chinese researchers should focus on improving model robustness and predictive power for large geographic areas and long time period. Investigations of large spatial and temporal scales exist in the western countries. For example, Cornell University scientists launched in 2004 a full-scale study on the impact of climate on mosquito population. Their goal was to develop a system for predicting and monitoring the transmission risk of mosquito vectors for West Nile virus, hoping to provide a mechanism for early warning of West Nile virus risk and serve as a model for other vector-borne diseases (Chronicle, 2004). Selecting the appropriate climate model is critical for the projection of DF transmission. In addition to downscaling climate model projection from global scale to a country or regional level, multi-model ensemble can reduce the uncertainties induced by the climate system models' internal variability (IPCC, 2014b). A study in Europe estimated DF epidemic potential using vectorial capacity based on historic and projected climate model data, and the result showed mitigating greenhouse gas emission can reduce the epidemic potential of DF in Europe (Helmersson et al., 2016). Similar studies that incorporate outputs from climate model and mosquito model to predict the spatiotemporal patterns of DF risk in China is certainly of high need. Given the size of China, we can define the potential epidemic risk for DF in China into different grades under different scenarios, and different zones can be identified as being "highly infectable", "infectable", "sensible", and "non-sensible" regions for preventing and managing possible DF outbreaks.

To better prepare China to face potentially more severe DF outbreaks and even epidemics, national-level efforts along a few directions are necessary. First, there is a need for a comprehensive climate change projection incorporating both the historical and future spatial scenarios, especially those can report on temperature, precipitation, humidity, etc. Existing studies on climate change in China focus mostly on one or a few climate factors (Feng et al., 2011; Wang and Chen, 2014; Zhou et al., 2014a). In the United States, the Environment Protection Agency led a series of nation-wide projects since 2010 to report data on various climate factors and a total of 37 indicators related to the causes and effects of climate change (EPA, 2016). There is a clear need for a study of such in China. Second, a complete estimation is needed for the overall distribution range and population of both *Aedes albopicus* and *Aedes aegypti* in China. Our literature survey identified only one study that projected the range of suitable habitats for *Aedes albopicus* under current and future climate situations (Fan, 2013). *Aedes aegypti,* the other important vector for DF, and a mosquito species widespread in the provinces in south China, including Guangxi, Yunnan, Hainan provinces and Taiwan, has not been studied in this aspect. The spatiotemporal distribution of mosquitoes can be used as a good predictor for the distribution of DF virus and thus DF health risk. China needs to systematically model and predict mosquito distribution and population throughout the whole country, similar to the United States Centers for Disease Control and Protection that predicts the potential range of Zika virus based on mosquito distribution range (CDC, 2016). Third, a nation-wide plan for DF prevention and DF outbreak management must be connected to DF health risk assessment and prediction, which should be developed based on national-scale comprehensive climate model and mosquito model. The health risk assessment must dynamically reflect the changes from climate and mosquito modeling, and it will be used to guide operations for DF prevention and outbreak control.

Regarding with scientific research and public health management related to DF and climate change in China, we recommend the following. First, more advanced research on the relationship between extreme weather events and DF should be encouraged. Extreme weather events show sudden and dramatic changes in weather conditions, making it more complicated to comprehend and predict its impact on DF. Second, it is necessary to develop more robust and region-specific weather-based DF model, mosquito model and climate model for the south and southeast parts of China considering that these places are high-risk regions for DF occurrences. Third, interdisciplinary collaboration should be encouraged. The marriage of climatology and epidemiology (Xu et al., 2017) will produce a more thorough understanding of the transmission of DF driven by climate change. World Health Organization and World Meteorological Organization co-led a comprehensive project examining case studies on how climate services can be applied for health management (WHO/WMO, 2016). Similar efforts are needed in China to support interdisciplinary teamwork to incorporate knowledge advancement in climate research into efforts for preparing communities from different regions in China for DF. Finally, research on strategies to build health culture and practice (including appropriate adaption) is in need at different scales and for different regions. Proactive adaptation strategies, policies and measures need to be identified and implemented by regional and national governments, and at household and individual levels.

6. Conclusion

This review paper summarizes the status of research regarding understanding, modeling and predicting the impact of climate change on DF in China. Climate change includes both long-term changes in climate factors and changes in frequency and magnitude of extreme weather

events. Climate factors (e.g. temperature, precipitation, humidity, wind velocity, and air pressure) may affect DF through impacting its three essential bioecological aspects: DF virus, mosquitoes and transmission environment. The effects of climate change on DF were found to be varied spatially and temporally. Empirical studies have confirmed that even limited changes in climate factors may alter the spatiotemporal distributions of DF. Weather-based DF model, mosquito model and climate model are essential for the projection of DF considering climate change. Unique challenges exist for the three modeling aspects in China.

Besides climate factors, other factors can influence the distribution of DF. Importation of DF cases, urbanization and anthropic program were found in literature to present additional challenges for DF prevention and control. Conversely, humans can play a very active role in controlling and preventing DF by spraying pesticides and using mosquito repellant as well as monitoring systems. In addition, improvement in weather-based DF model, mosquito model and the climate model may help increase the accuracy of DF projection. As for national level efforts for DF management, we recommend three major directions to pursue: 1) to build national-scale comprehensive climate change models and conduct regional-specific prediction of changes in climate factors, 2) to develop comprehensive mosquito range prediction that reflects national-scale climate change scenarios, and 3) to establish national or regional scale DF risk assessment and DF prevention strategies that are dynamically linked to climate models and mosquito models. Finally, we propose four recommendations for future work on climate and DF in China: 1) to encourage more advanced research on the relationship between extreme weather events and DF, 2) to develop regional-specific models for climate change, mosquito distribution and DF transmission for the high risk regions of DF in south China, 3) to promote interdisciplinary collaboration between climate studies and health services, and 4) to enhance public health education and management at national, regional and local levels.

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Appendix A. Supplementary data

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